82663.docx

Observational Study

External Validation of the Moroccan Arabic version of the EORTC Colorectal (CR29) module: monocentric study

External validation of the Moroccan Arabic EORTC QLQC-R29

Abstract

BACKGROUND

Quality of life outcomes are a focal endpoint of cancer treatment strategies.

AIM

We aim to externally validate the Moroccan Arabic version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Colorectal cancer patients (EORTC QLQ CR-29).

METHODS

Both Moroccan Arabic modules of QLQ CR-29 and QLQ C-30 were administered to Moroccan colorectal cancer (CRC). Psychometric properties were retested by measuring Cronbach's alpha coefficient for reliability and Intraclass correlation coefficient(ICC) to examine test-retest reproducibility. The multitrait-scaling analysis was performed to demonstrate the validity of the instrument and known-groups comparison was used to test the score's ability to discriminate between different groups of patients.

RESULTS

In total, 221 patients were included in our study and 34 patients completed the questionnaire twice. The urinary Frequency scale and Stool Frequency scale had good internal consistency with alpha Cronbach coefficients of 0,79 and 0,83 respectively, while the same coefficients were moderately lower for the Blood and Mucus in Stool scale (0,61) and the Body Image scale (0,67). The ICCs ranged from 0,88 to 1 indicating good to excellent reproducibility. In multitrait scaling analyses, the criterion for item convergent and divergent validity was satisfactory. The known-group comparison showed statistically significant differences between patients according to age, gender, stoma status, tumor location, and radiotherapy.

CONCLUSION
The Moroccan Arabic version of the EORTC QLQ-CR29 is a valid and reliable tool that can be used safely for research and clinical purposes in Moroccan CRC patients.

Key Words: Rectal neoplasm; Colorectal cancer; Health-related quality of life; Patient reported outcome measures; EORTC QLQ-CR29; EORTC QLQ-C30

Bachri H, Essangri H, El Bahaoui N, Benkabbou A, Mohsine R, Majbar AM, Souadka A. External Validation of the Moroccan Arabic version of the EORTC Colorectal (CR29) module: monocentric study. *World J Methodol* 2023; In press

Core Tip: Patient related outcomes such as quality of life are a focal endpoint of cancer treatments strategies. Many QoL questionnary are not trully validated. We aim to externally validate the Moroccan Arabic version of the EORTC QLQ CR29 on larger and more heterogenous population in order to affirm its validity and reliability in arabic colorectal cancer patients.

INTRODUCTION

Colorectal cancer (CRC) is a global challenge [1]. However, even with an increasing incidence, the implementation of screening programmes and the large array of advanced treatment modalities has significantly reduced mortality [2,3]. Nonetheless, colorectal cancer survivors suffer impaired physical and bowel functions, as well as psychological symptoms such as anxiety, sleep disruption, and depression [4]. All together, these symptoms negatively reflect on the quality of life [5] and makes looking beyond oncological outcomes of great importance.

Health-related quality of life (HRQL) is an abstract and multidimensional concept [6] which can be assessed by the European Organization for Research and Treatment of Cancer (EORTC) questionnaires. Core measurement tools examine issues common to different cancer sites and can be used as a stand-alone questionnaire or in combination with disease specific modules [7]. The EORTC QLQ-CR29 questionnaire specific to colorectal cancer and its psychometric properties have been tested in several languages and contexts. [8–16]

Recently, The QLQ-CR29 has just been only translated for Moroccan Arabic dialect. [17] However this adaptation was performed on a very limited sample size of 120 patients under the usual requests of the EORTC organization. The aim of this study is to externally validate this version and assess its psychometric properties on larger Moroccan colorectal cancer patients.

MATERIALS AND METHODS

We followed the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) directive guidelines for observational studies [18]. The Approval of the study protocol was obtained from the institutional ethics review board (number : 79/17) and all patients enrolled in the study provided a written, informed consent allowing the use of their data for clinical studies at the time of their initial visit.

Description of the instruments

The participants completed a general information section including sociodemographic and clinical data, alongside both the Moroccan Arabic module of EORTC QLQ-CR29 [17], and the validated Moroccan Arabic version of the QLQ-C30 (version 3.0). [19]

The EORTC QLQ-C30:

The EORTC QLQ-C30 includes five functional subscales (i.e., physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning), three symptom subscales (i.e., fatigue, nausea and vomiting, and pain), a global QoL subscale, and six single symptom items (i.e., dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). The scoring of items is on a 1 to 7 and 1 to 4 Likert scales for the global health status/quality of life and the other scales. High scores represent better functioning and worse symptoms. [20][21]

The EORTC QLQ-CR29:

The morocan arabic module of EORTC QLQ-CR29,[17] is a colon and rectum site-specific quality of life module with 29 items consisting of 4 multi-item scales (body image, urinary frequency, blood and mucus in stool, and stool frequency) and 17 functional/symptomatic single-items (sexual interest, urinary incontinence, dysuria, abdominal pain, buttock pain, bloating, dry mouth, hair loss, taste, flatulence, fecal incontinence, sore skin, embarrassment, stoma care problem, impotence or dyspareunia). Among these items, only body image, anxiety, weight, and sexual interest are functional scales.

The eighteenth item (Q18) is an indicator of colostomy/ileostomy construction, while the following items are separately arranged for patients with a stoma (Q19-Q25) and without (Q19-Q25) according to symptoms of stool frequency, flatulence, fecal incontinence, sore skin and embarrassment while item 25 is specific for stoma care. Sexual interest, impotence and dyspareunia items are categorized according to gender with the corresponding questions being Q26-Q27 and Q28-Q29 for male and female respondents respectively. All questionnaire items ask about the past week except the ones on sexuality, which request the patients to evaluate the past four weeks. As regards the

scoring, the multi-item scales and single items are scored using a 1 to 4 point Likert scale ("not at all", "a little", "quite a bit", "very much") with the highest score representing the best functional status or the worst symptom [22].

Study population and data collection :

Patients were prospectively recruited from the national oncology institute during the period between November 2019 and January 2020.[23,24] Patients aged over 18 years old, with pathologically confirmed colon and/or rectum cancer and who underwent surgery at least 6 mo prior to the enrollment in the study were included. Patients were excluded if they were unable to understand the questionnaire, had cognitive and/or medical complications that hindered the interview completion and those who submitted an incomplete questionnaire. Participants were either approached during follow up visits or contacted *via* telephone. Patient's characteristics were reported according to age, gender, stoma status, cancer location (colon *vs* rectum), neoadjuvant radiochemotherapy and adjuvant chemotherapy.

As the sample size determination for psychometric validation studies lacks clear recommendations [25], we determined the required sample by allocating a number of observations 5 to 10 times greater than the variables.[26] Accordingly, the sample needed size ranged between 150 and 300 participants in order to externally validate this version.

Statistical Analysis:

The scores for the QLQ-CR29 and the QLQ-C30 questionnaires were linearly converted into 0 to 100 point scores according to the standard EORTC guidelines. [20] Descriptive statistics were generated through mean, median, standard deviation (SD), and floor and ceiling effects, while age was categorized in 3 groups: < 40 years ; 41- 65 years and > 65 years.

In order to proceed to the external validation of the Moroccan Arabic module of de QLQ-CR29 we followed the identical steps of a first validation in a totally different population. There are two different levels of reliability, namely internal consistency and

reproducibility. Internal consistency reliability was determined using Cronbach's alpha coefficient with a score greater than 0,7 considered acceptable, above 0,8 was good and higher than 0,9 was considered excellent.

A random subgroup of patients was selected to retake the QLQ CR-29 questionnaire after 7 to 14 days from the first interview in order to examine the test-retest reliability. The results of the two measurements were assessed using the Intraclass correlation coefficient (ICC) and an ICC score of 0,7 or higher was considered acceptable.

We tested the construct validity of the EORTC QLQ-CR29 using multitrait scaling analysis. [27] Convergent validity was examined by correlating each item with its own scale with an item-scale correlation of ≥0.40 equivalent to high correlation. Divergent validity on the other hand was tested by demonstrating that the item correlated higher with its own scale than with the others.

Concurrent validity was examined by comparing the scores of the QLQ-CR29 and the QLQ-C30 using Pearson's correlation.

Clinical validity was assessed using known group comparison through the Mann Whitney U test to examine the QLQ-CR29' ability to differentiate clinically distinct patients. Subgroups were categorized according to : age (<65 years *vs* ≥65 years), gender (male *vs* female), stoma status (permanent *vs* no stoma), tumor site (colon *vs* rectal) and neoadjuvant radiotherapy (no *vs* yes). All statistical analyses were performed using SPSS 26.0 (SPSS Inc., Chicago,IL, USA). Statistically significant results were defined with a P < 0.05 .

RESULTS
Patients Characteristics:

The sociodemographic and clinical characteristics of the patients enrolled in the study are detailed in Table 1. In total, 221 of 250(88,4%)patients completed the questionnaire among which 123 were males and 98 were females. The mean age of our patients was 55,6 ±12,7years. Seventy-eight (35,9%) participants had colonic cancer and 138 (64,1%) had rectal cancer of wich 89(64%)received neoadjuvant chemoradiotherapy, while 50 patients had a stoma (22,6%). Missing items were only associated with sexual problems with a miss rate of 9% for males and 23% for females.

Table 2 summarizes the distribution of the EORTC QLQ CR-29 and QLQ-C30 scores. The mean score for the different dimensions of the QLQ CR-29 ranged from 16,44 to 75,56 with the items "Hair loss" and "Weight" scoring the lowest and highest respectively. The percentage of respondents at floor was high (>50%) in 12 areas while the percentage of respondents at ceiling was high (>50%) in 1 item. The range of scores was broad in 21 dimensions except for the bag change it ranged from 0 to 83.

Reliability :

The internal consistency of the EORTC QLQ-CR29 reached the 0.7 criterion showing good consistency for the urinary frequency scale (0,79) and stool frequency scale (0,83), while for the blood and mucus (0,615) and the body image (0,672) scales the alpha Cronbach coefficient was slightly below the criterion (0.7). The Cronbach's alpha coefficient was higher for patients without stoma compared to those with stoma, except for the body image scale (0,64 with *vs* 0,69 without) which indicates higher reliability for patients without a stoma. More details are shown in Table 3.

Thirty four patients took the Arabic version of the QLQ-CR29 and for each item, the ICCs ranged from 0,889 to 0,999 indicating good to excellent reproducibility.

Construct validity :

All items exceeded the 0,40 criterion for item-scale convergent validity. Similarly, items correlated better with their own scales than with others which shows good divergent validity. Details of the multitrait scaling analysis are shown in Table 3. `

Concurrent Validity :

Correlations between the scales of the QLQ-CR29 and QLQ-C30 were low (r < 0.40). However, some areas with more related content showed higher correlations (r > 0.40), namely body image and social functioning. The abdominal pain scale also had a good correlation with the QLQ-C30 pain scale and stoma care problems were correlated to the global quality of life scale. In addition, most functional scales of the QLQ-CR29 were positively correlated with functional scales of the QLQ-C30 and negatively correlated with symptom scales of the QLQ-C30, while most symptom scales of the QLQ-CR29 were positively correlated with symptom scales of the QLQ-C30 and negatively correlated with functional scales of the QLQ-C30 as detailed in Table 4.

Clinical Validity:

The EORTC QLQ-CR29 allowed the distinction between patients based on differences between known groups. Table 5 and Table 6

Differences in the scores of patients with stoma were noted as they presented significantly more anxiety and body image issues. Males with stoma reported higher symptom scores for the "impotence" scale.

The participants with rectal cancer had worse QoL than those with colon cancer and male patients with rectal cancer had significantly higher symptom scores for flatulence, fecal incontinence, sore skin around the anus, stool frequency, defecation problems, and sexual dysfunction.

In addition, patients who received neoadjuvant radiotherapy had significantly higher symptom scores and more problems related to blood and mucus, buttock pain, bloating, stoma care problems, flatulence, fecal incontinence, sore skin, stool frequency, embarrassment and defecation problems.

Furthermore, the QLQ-CR29 showed differences between age groups with younger patients found to suffer more from defecation problems, stool frequency and embarrassment.

DISCUSSION

Health-related quality of life (HRQL) in CRC is an important component in both day to day practice and clinical research, therefore the proper assessment of patients' HRQOL is crucial [28]. This study showed that the Arabic version of the EORTC QLQ-CR29 questionnaire has good internal consistency, test-retest reliability and validity and is therefore valid and reliable to assess the quality of life of Moroccan colorectal cancer patients.

The internal consistency of the Arabic EORTC QLQ CR-29 demonstrated satisfactory results for the urinary frequency scale and stool frequency scale, with higher reliability scores for patients without a stoma which is similar to the Chinese validation [14]. As regards the blood and mucus and the body image scales, the alpha Cronbach coefficients were acceptable which was the case in other similar studies. [12,29] On the other hand, as suggested by Arraras et al[12], some differences may be due to the fact that the EORTC original validation was conducted on an international sample with high variance, while the Spanish validation concerned a more homogenous sample which may impact the alpha Cronbach coefficient.

The ICCs of our study were all greater than 0.8, thus indicating good to excellent reproducibility for both single item and multi-item scales. The Reliability coefficients were higher in our study than those reported by the Dutch validation [10] and mostly similar to those in the original psychometric validation study. [8] As such, the Moroccan Arabic translation of the QLQ CR-29 is a stable instrument.

The multitrait analysis confirmed the structure of all scales, which proves that the Moroccan Arabic translation of the QLQ-CR29 has a valid construct.

In the assessment of concurrent validity, correlations between the scales of the QLQ-C30 and the QLQ CR-29 were mostly low (<0.4) indicating that the two questionnaires measure different concepts. Few areas with related content had higher correlation scores which was expected given the similar concepts of these particular scales. Nonetheless, the results show that the two questionnaires are independent.

In terms of clinical validity, we found less significant differences related to stoma status than the original study [8]. Moreover, patients with colon cancer had a better function and

fewer symptoms, including sexual interest in males and stool frequency as opposed to rectal cancer. Interestingly, patients with rectal cancer and a stoma experienced more embarrassment with borderline significance (P = 0.053). When comparing age groups, younger patients reported worse symptoms than older patients.[30] Similar results were reported by the Dutch and Spanish Validation studies [10,12]. In addition, the particularities of the Moroccan population may be contributing to elderly patients' display of better resilience, QoL satisfaction, relatively better acceptance and the aforementioned results. Consequently, the QLQ-CR29 was found to discriminate between age groups.

A higher missing data rate was registered for sexual dimensions compared to others as patients were more reticent about answering sex-related questions which makes their interpretation more difficult. Similar observations were made in the Chinese and Iranian studies, which hindered discussions regarding sexual activity and even ostomy. [14,16] Nonetheless, providing explanations to patients when answering the questionnaire was noted to help. In our context, this issue may be explained by the cultural and religious particularities of the Moroccan population where sexual practices are taboo. [31] More studies addressing this problem should be conducted to determine the reliability and validity of the CR-29 in evaluating the sexual aspects of QoL for patients according to cultural contexts.

This study has some limitations, one of which is the limited sample size of patients. However, the minimum sample size was set at one hundred and fifty patients according to EORTC organization and other EORTC QLQ-CR29 validations were performed on a smaller population such as El Alami's.[17] Self-administration was not possible due to the high level of illiteracy in our context; consequently, patients received the help of one of the investigators who was in charge of reading the questions and different options for the answer. Furthermore, although the use of confirmatory factor analysis may be an option, multitrait scaling analysis is the most frequently used method for the EORTC tools' transcultural validations.[21] Notwithstanding the foregoing, this study clearly validate the Moroccan Arabic validation of the EORTC QLQ-CR29 questionnaire which will allow the correct evaluation of HRQOL of colorectal cancer patients.

CONCLUSION

To summarize, the psychometric properties of the Moroccan Arabic version of the EORTC QLQ CR-29 show that it's a reliable and valid instrument to measure the quality of life of colorectal cancer patients and could be used to complement the EORTC QLQ-C30 in assessing HRQOL. Conducting more transcultural validations and standardizing patient-reported outcome questionnaires, especially in the field of oncology, will allow us to broadly assess cancer therapy outcomes and weigh the benefits against the quality of life impact.

ARTICLE HIGHLIGHTS

Research background

Health-related quality of life (HRQL) is an abstract and multidimensional concept [6] which can be assessed by the European Organization for Research and Treatment of Cancer (EORTC) questionnaires. Core measurement tools examine issues common to different cancer sites and can be used as a stand-alone questionnaire or in combination with disease specific modules

Research motivation

The EORTC QLQ-CR29 questionnaire specific to colorectal cancer and its psychometric properties have been tested in several languages and contexts. [8–16]

Recently, The QLQ-CR29 has just been only translated for Moroccan Arabic dialect. [17] However this adaptation was performed on a very limited sample size of 120 patients under the usual requests of the EORTC organization.

Research objectives

The aim of this study is to externally validate this version and assess its psychometric properties on larger Moroccan colorectal cancer patients.

Research methods

The scores for the QLQ-CR29 and the QLQ-C30 questionnaires were linearly converted into 0 to 100 point scores according to the standard EORTC guidelines. [20] Descriptive statistics were generated through mean, median, standard deviation (SD), and floor and ceiling effects, while age was categorized in 3 groups: < 40 years ; 41- 65 years and > 65 years.

In order to proceed to the external validation of the Moroccan Arabic module of de QLQ-CR29 we followed the identical steps of a first validation in a totally different population. There are two different levels of reliability, namely internal consistency and reproducibility. Internal consistency reliability was determined using Cronbach's alpha coefficient with a score greater than 0,7 considered acceptable, above 0,8 was good and higher than 0,9 was considered excellent.

A random subgroup of patients was selected to retake the QLQ CR-29 questionnaire after 7 to 14 days from the first interview in order to examine the test-retest reliability. The results of the two measurements were assessed using the Intraclass correlation coefficient (ICC) and an ICC score of 0,7 or higher was considered acceptable.

We tested the construct validity of the EORTC QLQ-CR29 using multitrait scaling analysis. [27] Convergent validity was examined by correlating each item with its own scale with an item-scale correlation of ≥0.40 equivalent to high correlation. Divergent validity on the other hand was tested by demonstrating that the item correlated higher with its own scale than with the others.

Concurrent validity was examined by comparing the scores of the QLQ-CR29 and the QLQ-C30 using Pearson's correlation.

Clinical validity was assessed using known group comparison through the Mann Whitney U test to examine the QLQ-CR29' ability to differentiate clinically distinct

patients. Subgroups were categorized according to : age (<65 years *vs* ≥65 years), gender (male *vs* female), stoma status (permanent *vs* no stoma), tumor site (colon *vs* rectal) and neoadjuvant radiotherapy (no *vs* yes). All statistical analyses were performed using SPSS 26.0 (SPSS Inc., Chicago,IL, USA). Statistically significant results were defined with a $P < 0.05$.

Research results

In total, 221 patients were included in our study and 34 patients completed the questionnaire twice. The urinary Frequency scale and Stool Frequency scale had good internal consistency with alpha Cronbach coefficients of 0,79 and 0,83 respectively, while the same coefficients were moderately lower for the Blood and Mucus in Stool scale (0,61) and the Body Image scale (0,67). The ICCs ranged from 0,88 to 1 indicating good to excellent reproducibility. In multitrait scaling analyses, the criterion for item convergent and divergent validity was satisfactory. The known-group comparison showed statistically significant differences between patients according to age, gender, stoma status, tumor location, and radiotherapy.

Research conclusions

The Moroccan Arabic version of the EORTC QLQ-CR29 is a valid and reliable tool that can be used safely for research and clinical purposes in Moroccan CRC patients.

Research perspectives

This tool can safely be used in research and clinical purpose and can be also used in the validation of other PROM tools.

82663.docx

ORIGINALITY REPORT

52%

SIMILARITY INDEX

PRIMARY SOURCES

1	www.researchsquare.com Internet	1904 words — 51%
2	www.ncbi.nlm.nih.gov Internet	24 words — 1%